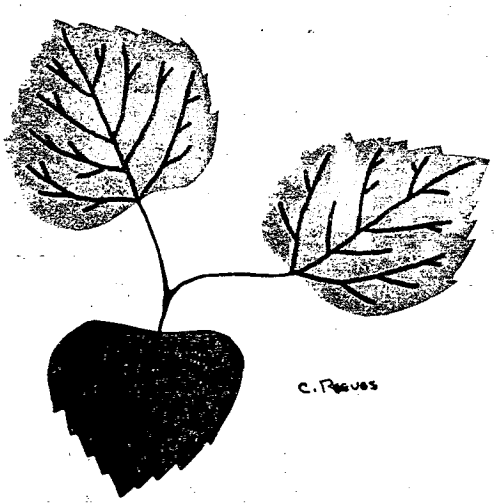
THE PULMONARY CIRCULATION

Conference III
The Control of Cellular Proliferation in the Pulmonary Circulation

In Honor of Robert F. Grover, M.D., Ph.D.

September 19th-22nd, 1988

Lost Valley Ranch
Deckers, Colorado



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THE PULMONARY CIRCULATION

Conference III
Pulmonary Vascular Reactivity

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Introduction

The Grover Conferences on the Pulmonary Circulation are named in recognition of the many contributions of Dr. Robert Grover, M.D., Ph.D., to our understanding of the physiology and pathophysiology of the pulmonary vasculature. He has performed a wide variety of animal laboratory experiments and clinical investigations. His studies of brisket disease in cattle at high altitudes were among the first (1960) and were certainly the most complete descriptions of chronic hypoxic pulmonary hypertension. He investigated species differences in the pulmonary circulatory responses to high altitude of cattle, sheep, rabbits, cats, llamas, dogs, rats, guinea pigs, pigs; 1960-1976. He was involved in evaluating many factors which influence acute and chronic hypoxic pulmonary hypertension (sympathetic activity, 1968; prostaglandins, 1974-1976; endotoxin, 1974-1976; calcium agonists, 1974; mast cells and histamine, 1974-1976; acetylcholine, 1976; unilateral pulmonary artery ligation, 1978; ethyl alcohol, 1978; platelets, 1976; genetic factors, 1974; 48/80, 1977; cold exposure, 1975-1978.

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Dr. Grover was the first to demonstrate that pulmonary hypertension in congenital heart disease can have a reversible component (1961). He made the first measurements of pulmonary arterial pressure in normal North American residents of high altitude (1963) and he showed the reversibility of pulmonary hypertension, when it was observed (1966). He was involved in the first measurements of pulmonary vascular reactivity in pregnant women (1975). The first measurements of pulmonary vascular reactivity in subjects susceptible to high altitude pulmonary edema were made by him (1971), and he stimulated studies of high altitude pulmonary edema in children at Leadville, Colorado (1979, 1980).

The concept of having a conference on the Pulmonary Circulation arose because there was no ongoing forum in North America dedicated to the study of the pulmonary vasculature. It is intended that such a conference will be held every second year. The first conference took place here in Deckers in 1984 and focused on pulmonary vascular reactivity. The second conference focused on the lipid mediators in the pulmonary circulation. Both meetings were attended by approximately forty scientists who made full use of the opportunity to exchange information and ideas. This meeting is designed to explore the control of cellular proliferation in the pulmonary circulation. Chronic pulmonary hypertension is a highly fatal human disorder. The mortality is largely the result of proliferation in and around the vessel wall which obstructs the lumen and reduces blood flow. Blood elements, endothelium, media, adventitia, and even surrounding lung tissue participate in a proliferative process and these elements interact with each other in complex ways. A better understanding of the processes involved is necessary before we can effectively treat pulmonary hypertensive disorders. In order to achieve a better understanding, the conference brings you together as leading researchers who have studied proliferative processes from the perspective of your respective disciplines.

In the next four days we hope to utilize this isolated conference facility and our format to promote cross-

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fertilization of ideas and collaboration between workers of very different backgrounds. It is our hope that the interchange of concepts and information fostered by this setting will lead to better definition and treatment of the disorders of the pulmonary circulation.

Welcome to the third Grover Conference on the Pulmonary Circulation: "The Control of Cellular Proliferation in the Pulmonary Circulation."

E. Kenneth Weir, M.D.
John T. Reeves, M.D.

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PROGRAM AGENDA

Monday, September 19, 1988

"The Control of Cellular Proliferation in the Pulmonary Circulation."

8:15 AM	WELCOME E. Kenneth Weir, M.D.
Chairmen:	John T. Reeves, M.D. and John A. Bevan, M.D.
	"Regulation of vascular cell growth and differentiation."
8:20	Peter B. Bitterman, M.D., Associate Professor of Medicine - (Overview).
	Control mechanisms for cellular hypertrophy and hyperplasia.
9:00	Drew Noden, Ph.D., Professor of Anatomy, - The cellular embryology of the craniofacial and pulmonary vasculature.
9:20	DISCUSSION
9:40	Alicia Orlidge, Ph.D., Research Fellow - Influence of pericytes on capillary endothelial cell growth.
10:00	DISCUSSION
10:20	BREAK
10:40	William E. Benitz, M.D., Assistant Professor of Pediatrics - The role of endothelial-smooth muscle communication in growth regulation.

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11:00 DISCUSSION

11:20 Robert Auerbach, Ph.D., Professor of Zoology -
Variation in endothelial function between organs.

11:40 DISCUSSION

12:00 LUNCH

Chairmen: Norbert F. Voelkel, M.D.
Bruce R. Zetter, Ph.D.

"Stimuli for growth in the vessel wall."

3:50 PM Mark N. Gillespie Ph.D., Associate Professor of Pharmacology -
Polyamines and lung cell responses in pulmonary hypertension.

4:10 DISCUSSION

4:30 Rosemary D. Bevan, M.D., Associate Professor of Pharmacology -
Adrenergic innervation and the control of structure and growth in vascular smooth muscle.

4:50 DISCUSSION

5:10 BREAK

5:20 Thomas N. Wight, Ph.D., Associate Professor of Pathology -
Proteoglycans in vascular cell proliferation and migration.

5:40 DISCUSSION

6:00 Harold F. Dvorak, M.D., Professor of Pathology -
Leaky vessels, fibrin, and tumor stroma generation.

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6:20 DISCUSSION

6:40 DINNER

Tuesday, September 20, 1988

Chairmen: Kurt R. Stenmark, M.D.
Alan Tucker, Ph.D.

"Regulation of matrix synthesis."

8:20 AM John A. McDonald, M.D., Ph.D., Associate Professor of Medicine - (Overview)

9:00 Robert P. Mecham, Ph.D., Associate Professor of Cell Biology and Medicine - Mechanisms of control in matrix protein synthesis.

9:20 DISCUSSION

9:40 David J. Riley, M.D., Professor of Medicine - Effects of mechanical forces on cell growth and the synthesis of extracellular matrix.

10:00 DISCUSSION

10:20 BREAK

10:40 Anita Roberts, Ph.D., Senior Scientist, National Cancer Institute - Growth factor modulation of matrix phenotypes.

11:00 DISCUSSION

11:20 Daniel B. Rifkin, Ph.D., Associate Professor of Cellular Biology - Regulation of matrix degradation.

11:40 DISCUSSION

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12:00 LUNCH

AFTERNOON FREE

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Wednesday, September 21, 1988

Chairmen: Ivan F. McMurtry, Ph.D.
Stephen L. Archer, M.D.

"Signal transduction in cellular activation"

8:20 AM	Thomas F. Deuel, M.D., Professor of Medicine - (Overview)
9:00	Peter Libby, M.D., Associate Professor of medicine - Interleukin-1 as a regulator of the proliferation of vascular wall cells.
9:20	DISCUSSION
9:40	Tommy A. Brock, Ph.D., Assistant Professor of Pathology - The role of inositol phosphate metabolism in cellular activation in vascular endothelium.
10:00	DISCUSSION
10:20	BREAK
10:40	Richard F. O'Brien, M.D., Assistant Professor of Medicine The role of protein kinase C in vascular smooth muscle proliferation.
11:00	DISCUSSION
11:20	David Madtes, M.D., Assistant Professor of Medicine Production and transduction of PDGF.
11:40	DISCUSSION
12:00	LUNCH

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Chairmen:		John V. Weil, M.D. John A. McDonald, Ph.D., M.D.
3:40		INTRODUCTION
3:50		Bruce Zetter, Ph.D., Associate Professor of Physiology - Tumor-blood vessel interactions in pulmonary metastasis.
4:10		DISCUSSION
4:30		Gary K. Owens, Ph.D., Associate Professor of Physiology - Mechanisms of smooth muscle cell growth in systemic hypertension: role of cellular hypertrophy versus hyperplasia.
4:50		DISCUSSION
5:10	BREAK	
5:20		David Knighton, M.D., Assistant Professor of Surgery - Macrophage-derived growth factors in wound healing.
5:40		DISCUSSION
6:00		John N. Evans, Ph.D., Associate Professor of Physiology and Biophysics - Changes in vessel structure as a determinant of hemodynamics.
6:20		DISCUSSION
6:40	DINNER	

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Thursday, September 22, 1988

Chairmen: Robert F. Grover, M.D.
E.K. Weir, M.D.

"Hemodynamics, treatment and regression in chronic pulmonary hypertension"

8:20 AM	Gwenda Barer, M.D., Reader in Medicine - Changes in reactivity in the presence of peripheral extension of pulmonary vascular smooth muscle.
8:40	DISCUSSION
9:00	Rosemary C. Jones, Ph.D., Assistant Professor of Pathology - Changes in cell growth and pulmonary vascular reactivity induced by hyperoxia.
9:20	DISCUSSION
9:40	Barbara Meyrick, Ph.D., Professor of Pathology - The sequence of cellular and hemodynamic changes induced by hypoxia and other stimuli.
10:00	DISCUSSION
10:20	BREAK
10:40	Walker A. Long, M.D., Senior Clinical Research Scientist - Results of the long-term use of prostacyclin in primary pulmonary hypertension.
11:00	DISCUSSION
11:20	Lynne M. Reid, M.D., Professor of Pathology - Overview and future directions.
12:00	Lunch and end of conference.

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